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EDITORIAL

On these pages the editor offers his opinions, unshackled by advertising patrons and unrestrained by anything save a sense of the decent and the truthful. The editor, alone, is responsible for their type, their tone and their tenor.

STATISTICS

SOME people take kindly to statistics. Others are annoyed by them and insist that if all statisticians were placed end to end they would not reach —a conclusion.

But those who implement horse sense into the assembling and interpreting of certain statistics find them useful both in diagnosis and treatment.

One does not have to believe that statistics are figures that may be made to prove anything—even the truth. It is so much easier to accept the great mass and mess of vital and futile statistics in good humor, and know that in this tonnage of gross and dross there will always be found a trace of the auric element.

And then statistics are often of real interest. There is in them so much that is helpful to the gentle art of conversation, so much of that kind of education which enables one to get into more intelligent trouble.

Many a dreary evening has been succored from boredom by quoting such merry bits of statistics, which may themselves be as futile as sky-writing in Pittsburgh, but have the saving grace of being entertaining.

And this contribution to entertainment alone justifies the labor and expense involved in achieving to them.

Personally, statistics cause us little annoyance, not even when they get personal.

For instance, we are only one-tenth of one per cent. worried over the finding that "one fisherman in a thousand drowns while fishing". And if and when we become that unfortunate *one* and theoretically one hundred per cent. involved, we shall be no longer interested in mundane statistics! So what?

But around the corner is the statistician's paradise. The Census will soon be on! And America expects that upon this day every

American citizen shall do his solemn duty, telling all that is to be told, and telling it with truth and with dispatch.

So that the reader may intensify his desire to treat the Census with sense and satisfaction, here are a few smug statistical statements which certainly should help us keep on living terms with ourselves.

An American has been defined as one who doesn't know the words of the "Star-Spangled Banner", and elsewhere as one who has both feet on the ground and both hands in the air.

And in the statistics appended is warrant enough for every American to wave and to rave with justifiable pride.

Viewed from a world standpoint the United States occupies not more than 6½ per cent. of the land surface and contributes a corresponding 6½ per cent. of the world population. In area and in people it is about one-fifteenth of the whole.

But the United States possesses 45 per cent. of the wealth of the world!

In its treasury lies 60 per cent. of the monetary gold in the possession of mankind. It has 17 billions of the 29 or 30 billions in all the world—20,000 tons of it, enough to load a freight train five miles long.

In this age it may be considered that oil lends more to dominance than any other material. Every year the world produces, in round figures, 2 billion barrels of oil. Census figures show that of this 2 billion barrels 1¼ billions, or 62 per cent., are produced in that 6½ per cent. of the world's surface that lies within the United States.

The one-fifteenth of the people of the world who live within the United States produce one-third of all the pig iron and of the steel that rivals oil in importance.

They mine 35 per cent. of the copper and the lead and the zinc; 30 per cent. of the world's coal.

Inexhaustible sulphur mines skirt the Gulf of Mexico. In Colorado there is the only mountain of molybdenum (used in hardening steel) in the world. California and New Mexico are now turning out the potash for the South's cotton crop which formerly came from Germany.

The United States consumes 45 per cent. of the world's tin, 56 per cent. of its rubber, 72 per cent. of its silk.

There are 43 million automobiles in the world and 29 million of them, 68 per cent., are in the United States.

The world has 41 million telephones and 20 million of them are in this American one-fifteenth of the world.

In the year 1937 the world produced 35 million bales of cotton. Of that total, 18 million bales, which is more than half the total, grew in the United States.

In a good year the world produces 5 billion bushels of wheat and the United States comes close to one billion, or a fifth of world production.

Four out of every 10 boxes that come to embrace yellow oranges in all the world have their covers tacked down in the United States. And 9 out of every 10 boxes of grapefruit.

The world produces around 5 billion pounds of coffee every year. Of this amount the United States consumes 1.7 billion pounds, which is 34 per cent.

There are more students in the colleges and universities of the United States than in those of all the rest of the world put together.

Americans are by far the best educated, best housed, best clothed, best fed people in all the world.

So say Statistics!!!

IVOR GRIFFITH.

Automobile Liquid Polish

A good liquid car polish can be made from:

White spirit	2½ pt.
Mineral oil	2½ pt.
Turkey red oil	4 pt.
Ammonia	1 oz.
Water	1 pt.
Glycerin	1 pt.
Formaldehyde	8 oz.
Fuller's earth	9 oz.
Bentonite	6 oz.

Mix the oils together, add the abrasive powders and then the water, glycerin and formaldehyde. Mix rapidly until a smooth product results.

ORIGINAL ARTICLES

SULFONATED OIL—COAL TAR DISINFECTANT MIXTURES
(Stability, Toxicity and Other Comments)

By Louis Gershenfeld and Bernard Witlin
Department of Bacteriology, Philadelphia College of Pharmacy and Science

IN a previous report (1), a method was presented for making water immiscible coal-tar disinfectants soluble in or miscible with water by mixing these phenolic substances in all proportions with 50 per cent. sulfonated castor oil. An analysis of the latter revealed a moisture content of 52 per cent. and the organic SO_3 content was 5.6 per cent. The *pH* on a 2 per cent. solution was 8.83. The phenol coefficients of old mixtures were determined against Eberthella typhi and compared with freshly prepared mixtures.

A comparative study is presented of such mixtures (old and freshly prepared mixtures), as to:

(*a*) Stability;

(*b*) Their phenol coefficients against Staphylococcus aureus and Eberthella typhi; and

(*c*) The relative toxicity of a freshly prepared mixture of U. S. P. Cresol with 50 parts of 50 per cent. sulfonated castor oil, *pH* 8.3-8.5, as compared with Liquor Cresolis Saponatus (2).

Experimental Investigation

The following five solutions were prepared two years ago. The Phenol Coefficients obtained by the United States Food and Drug Administration technique at that time were:

TABLE I

Disinfectant	Parts Bactericide cc.	Parts 50% Sulfonated Castor Oil cc.	Phenol Coefficient E. typhi, 20° C.
Cresol (U. S. P.)	50	50	2.20
o-Cresol	50	50	2.20
m-Cresol	50	50	2.45
p-Cresol	50	50	2.75
15% Tar-Acid Oil	50	50	3.30
Control	00	100	0.00

Physical Appearance

After standing at room temperature for two years, the mixtures were examined and the following characteristics noted:

TABLE II

Sulfonated Castor Oil with 50% of	Physical Appearance of Mixture
Cresol (U. S. P.)	Slightly darker in color. A small amount of white sediment was found at the bottom of bottle, which quickly resuspended upon agitation.
o-Cresol	Same
m-Cresol	Same
p-Cresol	Same
15% Tar-Acid Oil	No observable change

Upon mixing, the cresol solutions appeared slightly turbid, due to the sediment. This turbidity disappeared, as the solutions were warmed. All sulfonated castor oil-cresol mixtures gave clear solutions with water and mixed in all proportions. The sulfonated castor oil 15 per cent. tar-acid oil mixtures mixed in all proportions with water and gave the usual milky solutions.

Bactericidal Efficiency

Phenol coefficient tests were performed upon the two-year old mixtures, employing the United States Food and Drug Administration technique (3), using both Eberthella typhi and Staphylococcus aureus as the test organisms, at 20 degrees C.

Controls of freshly prepared 50 per cent. sulphonated castor oil-coal tar derivative mixtures were made from original samples of the water-immiscible coal-tar disinfectants, and these also were tested for their bactericidal efficiency.

TABLE III

50% Sulfonated Castor Oil with	Phenol Coefficients at 20° C. freshly prepared mixtures made November 4, 1939		Two-year old mixtures made November 4, 1937	
Disinfectant Mixture	S. aureus	E. typhi	S. aureus	E. typhi
Cresol (U. S. P.)	1.87	2.20	1.87	2.00
o-Cresol	2.13	2.20	2.13	2.20
m-Cresol	2.00	2.45	2.00	2.40
p-Cresol	2.13	2.75	2.13	2.75
15% Tar-Acid Oil	3.00	3.30	3.00	3.60

It was noted that there was no change in the phenol coefficients of these mixtures, kept for two years in cork stoppered soft glass bottles as compared to freshly prepared mixtures.

The bactericidal efficiency of Liquor Cresolis Saponatus was identical with that of a mixture of equal parts of sulfonated castor oil and cresol (U. S. P.).

Toxicity

Two per cent. solutions of the bactericide mixtures were made in sterile physiological saline. It was noted that the saline solutions containing the sulfonated castor oil-cresol were approximately only one-third as turbid as that prepared from the Liquor Cresolis Saponatus.

Rabbits weighing approximately 2.20 kilograms were injected intravenously with 20 cc. of the different 2 per cent. bactericide mixtures in saline solutions. Injections were given twice weekly for six weeks, with no apparent change observable in the rabbits.

Cresol With Other Sulfonated Oils

The bactericidal efficiencies of sulfonated oil-cresol mixtures with the following commercially available sulfonated oils were noted:

A. Sulfonated Castor Oil (50% oil content)
(This sample is different from the one mentioned above)
B. Sulfonated Castor Oil (75% oil content)
C. Sulfonated Sperm Oil
D. Sulfonated Olive Oil
E. Sulfonated Oleic Acid
F. Sulfonated Cocoanut Oil

The 50 per cent. Sulfonated Castor Oil (A) was the only one which produced a clear solution when mixed with equal parts of Cresol U. S. P. XI. The other oil-cresol mixtures produced turbid solutions with cresol and clouded or immiscible solutions when these mixtures were added to distilled water. The addition of sodium hydroxide to the oils (A to F incl.) to produce a higher *pH* (approx. neutral to Phenolphthalein) jelled the oils. It was therefore necessary to dilute the oil content one-third with distilled water, so as to obtain a free-flowing liquid. The 75 per cent. Sulfonated Castor Oil, Sperm Oil and Oleic Acid diluted with water and neutralized by

alkali remained clear when warm or cold. The neutralized and diluted Sulfonated Cocoanut Oil (F) remained turbid when warm or after cooling. The neutralized and diluted Sulfonated Olive Oil (D) was clear when warm but became clouded upon cooling.

Mixtures of the neutralized and diluted (to one-third) sulfonated oils and cresol (half and half) presented clear mixtures in the case of the Castor Oil (B), Sperm Oil (C) and Oleic Acid (E) when warm or cold. Tests by the FDA technique for the bactericidal efficiencies with the clear solutions presented the same phenol coefficients (as given above) regardless of the type oil employed.

Patents Issued and Other Comments

Before the publication of our original presentation (1), the literature for the past twenty-five years was examined. We were unable to find anything along the lines of our report in the American literature until our article appeared. Immediately after its publication, we received numerous comments and inquiries. Our observations were abstracted and they appeared in many periodicals. The "Drug Trade News" in the October 23, 1939, issue presented a detailed report of our findings. In the November 6, 1939 issue of the same publication, a statement commenting on the fact that patents have been issued for such soluble germicidal mixtures reads as follows:

> "Newark, N. J.—Use of sulfonated oils as dispersing agents for coal-tar disinfectants like cresol and thymol, as described in DRUG TRADE NEWS for October 23, 1939, page 34, with specific reference to sulfonated castor oil is covered by U. S. Patent 2,073,057, 'Water Soluble Bactericidals,' issued on March 9, 1937 and 1,930,474, 'Processes for Making Water Soluble Disinfectants,' issued on October 17, 1933, Dr. Paul Goedrich, here told DRUG TRADE NEWS last week. The patents were issued to Dr. Goedrich."

Shortly after the above article appeared we received a note from Dr. George Roeder, Rahway, N. J. He makes the following comments:

> "The solubility of phenols in sulfonated castor oil has been principally known for more than thirty years. Kurt Laubenheimer, in 1909 in a booklet 'Phenol und seine Derivate als Desinfektionsmittel' names Leibrecht, a technical chemist, as the

discoverer of the above fact. Laubenheimer himself, on pages 67 to 124 of his treatise describes in a very detailed study the bacteriological effect of many different phenols dissolved in sulfonated castor oil and diluted with water.

The earlier of the two above mentioned patents is applied for in Germany in 1926 and in U. S. A. one year later. It is obvious that a fact published in 1909 cannot be patented in 1926 or later. Indeed, the two patents are far from covering generally the use of sulfonated castor oil as a dispersing agent for phenols, but they consist only in some (very questionable) modifications in preparing those solutions."

We subsequently received notations from others, which were similar in their contents to the remarks made by Mr. H. Rothstein of the Apex Chemical Co:, Inc., of New York City, N. Y., which follow:

"It may interest you and yours to know that we have employed sulphonated castor oil to make coal tar disinfectants miscible with water for the past 20 years, so you see the subject is not really news to us."

We examined U. S. Patent 1,930,474, "Process for Making Water Soluble Disinfectants," for which application was made on July 7, 1927 by Paul Gödich of Munich, Germany, and the patent was issued on October 17, 1933. U. S. Patent 2,073,057 on "Water Soluble Bactericidals," for which application was made on April 6, 1933 was issued on March 9, 1937 to Paul Goedrich of Elizabeth, N. J. A British Patent 508,407 for which application was made on March 8, 1938 was issued on June 30, 1939. All of these patents cover subject matter related to our presentation.

Summary

1. The Phenol Coefficient of Water Immiscible Coal-Tar Disinfectants made miscible by mixing with 50 per cent. Sulfonated Castor Oil (adjusted to faint alkalinity to phenolphthalein), is unaltered upon standing for two years.

2. The Phenol Coefficient of Cresol made water miscible by the use of Sulfonated Castor Oil is the same as that of Liquor Cresolis

Saponatus, when containing the same amount of active ingredients (500 parts U. S. P. Cresol per 1000 parts of finished product).

3. The toxicity of cresol sulfonated castor oil mixtures is such as not to mitigate against their use externally on the body or for general household use.

4. The use of other sulfonated oils for making cresol water miscible is considered.

5. Various patents are discussed briefly. We personally do not comment on their validity, but present remarks by others.

Conclusion

Due to their bactericidal efficiency, economy and simplicity in preparation, stability, rapid miscibility with water in all proportions, and low toxicity, 50 per cent., sulfonated castor oil-cresol mixtures are advocated. Sulfonated castor oil is highly recommended for making cresol and other coal-tar disinfectants (which are immiscible with water) water miscible.

REFERENCES

(1) Gershenfeld and Witlin: *American Journal of Pharmacy*, Vol. 111, No. 8, p. 314, August, 1939.

(2) United States Pharmacopœia XI.

(3) Circular No. 198, Food and Drug Administration, United States Department of Agriculture, December, 1931.

Weed-Salad!!

Pioneer great-grandmother's "spring greens," made from all sorts of wayside weeds, were better than spinach when it came to providing vitamin C, it appears from a study reported in a recent issue of *Science* by Prof. R. C. Burrell and Miss Helena A. Miller, of Ohio State University.

Prof. Burrell and Miss Miller analyzed 15 kinds of weeds that have been used in cooked greens and salads, and found that most of them are superior to fresh spinach. Milkweed topped the list by far, with 6.556 milligrams of ascorbic acid per gram of fresh weight. Spinach averaged only 0.812 milligrams per gram, in comparison.

Other high scorers included pokeweed, dandelion, watercress, sorrel and skunk cabbage.

NEW PRECIPITATING AGENTS FOR ALKALOIDS AND AMINES

By Charles C. Fulton

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Saint Paul, Minnesota

IN "The Precipitating Agents for Alkaloids" (1) (1932), the writer gave a summary of then-existing knowledge of the reagents. The present article deals with advances made and adds 93 reagent formulas to the 91 previously given. Of these a very few are neither original nor new, but merely escaped inclusion in the preceding article; some others have been given by the writer in the interim, or at least referred to as they were developed, in connection with specific cases (2, 3, 4). The majority, however, are entirely new. The discussion, particularly that on precipitation from acids and the method of direct application, not only explains the advances made, but points the way to further and future advances of great importance.

Recognition of characteristic crystals under the microscope, the method of identification originated and developed by Behrens, Wormley, Stephenson, and others, is now conceded to be the best, most convenient, and most reliable means of identifying the pure alkaloids in drug analysis or toxicology. With a sufficient number and variety of reagents a good test can probably be found for *any* isolated (pure) amine, making possible its identification even in minute quantity.

The reagents are also sometimes used for separation of alkaloids from solution by precipitation, for separation of one alkaloid from another, for titration by precipitation, and of course for detection of the presence of alkaloids or amines.

The "alkaloidal reagents" actually precipitate amines in general, including ptomaines, basic dyes, proteins, etc.; some precipitate even ammonia and the heavier alkali metals; and some have now been found that (from phosphoric acid solution) precipitate amides as well, and *all amines,* even the simplest amino-acid, glycine, and the acidic amino-acids. The extreme importance in biological chemistry of amines, amides, amino-acids, and proteins needs no emphasis; even some "virus diseases" and "bacteriophages" are now considered specific proteins rather than living organisms.

Precipitation From Acids

In previously surveying the field, the writer mentioned precipitation from non-aqueous solutions (such as alcohol, chloroform, glycerine), and precipitation of the soluble free bases from aqueous solution by neutral reagents. Neither of these has assumed greater importance in the interim; nor do alkaline reagents seem to offer any great possibilities, although Nessler's reagent is useful. On the other hand really new departures of the utmost value have been found in the use of strong acids for the test drop; strong acetic, concentrated hydrochloric and hydrobromic, strong sulfuric, and syrupy phosphoric acids.

This development has come about gradually, chiefly by reason of a steadily increased use of hydrochloric acid, in various strengths, with attendant discoveries of valuable new crystal tests. The traditional "general alkaloidal reagents" are solutions of certain compounds (acids, salts or bases) in plain water, or in a few cases with just enough acid to prevent basic hydrolysis; and these were added to neutral or barely acidified solutions of the alkaloidal salts. In 1933 the writer introduced strong hydrochloric acid—25 per cent. by volume of concentrated HCl—as the solvent for a number of reagents in studying cocaine and novocaine (2), and a little later, with G. D. Williams, used concentrated hydrochloric acid as solvent for gold chloride and gold bromide in identifying heroin (3). These reagents were still used with plain water solutions of the alkaloidal salts. In 1935 the writer began using concentrated hydrochloric acid as a solvent for the alkaloid also; the very sensitive test of the beautiful gold bromide crystals given by morphine in a test-drop of concentrated HCl has recently been published (4).

At the Washington Laboratory Matchett and Levine developed an "Acid Wagner's reagent," made by treating iodine and KI with concentrated HCl, for use in identifying traces of morphine, down to 2 gamma (5).

Meanwhile the present writer had independently suggested (in an unpublished article) the use of "KI_3 in Concentrated HCl" for micro-crystal identification tests by direct application to morphine, codeine, dionine, and other alkaloids; and later published formulas for six I-KI reagents made with strong acids, devised for the identification of minute traces of morphine, down to 0.5 to 0.1 gamma (6).

I. S. Shupe, also working independently, has introduced 10 per cent. HCl (which is about 27 per cent. by volume of the concentrated

acid) as solvent for certain synthetics, acetanilid, acetphenetidin, and neocinchophen, in micro-crystal tests with phosphotungstic acid, Wagner's reagent, potassium thiocyanate, and chloroplatinic acid (7, 8a).

Amides, such as acetanilid and phenacetin, are neutral substances, and in the past have usually not been thought of as susceptible to precipitation by the "alkaloidal" or amine reagents. In solution in strong acid, however, their basic properties are enhanced, their acidic properties suppressed, and they show unmistakably their relationship to amines. The same kind of effect, though not so extreme, is obtained with certain recognized alkaloids, such as caffeine. This is a major aspect of the use of a strongly acid test-drop, but not the only one, since the acids differ greatly.

The solubility of precipitated compounds decreases with the acid used, in the order:

acetic acid
hydrochloric acid
(water)
sulfuric acid
phosphoric acid

Hydrochloric acid and sulfuric acid do not differ much from water in this respect, but the precipitates are far more soluble in acetic acid and far less in phosphoric acid. Hence precipitation of the simplest and most feebly basic compounds is most readily obtained in syrupy phosphoric acid.

Many new identification tests will be available without making new reagents, by applying the usual aqueous reagents to solutions of the alkaloids in various acids. In experimenting, first test the reagent for compatibility with the acid. Sometimes a little precipitation from the reagent can be disregarded (such as KCl precipitated from a reagent made with KI, when it is applied to a concentrated HCl solution). The acids the writer has used are as follows:

Acetic acid (2 plus 1). The glacial acid (2 parts) is diluted with water (1 part), otherwise it will spread all over the slide.

Concentrated Hydrochloric acid (36-37 per cent.).

Concentrated Hydrobromic acid (34 per cent. or 40 per cent.).

Sulfuric acid (1 plus 1). The concentrated acid diluted with an equal volume of water, in general, to dissolve the alkaloid. The actual test drop should not be stronger than 1 plus 3 for iodides, 2 plus 3 for bromides, or 1 plus 1 for chlorides.

Syrupy Phosphoric acid (85 per cent.).

Besides the above mentioned effects, hydrochloric and hydrobromic acids have a specific effect, due to their relationship to many of the reagents, which are complex chlorides, bromides, iodides, etc. This results in many new crystal tests with these particular acids.

As an illustration of the value of the new methods, the identification of physostigmine may be cited. In 1933 Glycart, having tried the usual aqueous reagents on aqueous solutions of physostigmine, reported to the Association of Official Agricultural Chemists that no suitable micro-chemical tests had been found for physostigmine (9).* Yet, if the physostigmine is dissolved in concentrated HCl instead of water, the addition of the usual gold bromide reagent (aqueous $HAuBr_4$) will give excellent crystals, as fine a microchemical test as could be desired; the addition of the usual gold chloride reagent (aqueous $HAuCl_4$) will give other excellent crystals; and platinum bromide (aqueous H_2PtBr_6), with a little stirring to start their formation, will also yield good crystals. Or, to a drop of aqueous solution of physostigmine add a full drop of Gold H Bromide in Concentrated HCl (Reagent No. 47 in this article), Gold H Bromide and HCl (No. 46), or Gold H Chloride in Concentrated HCl (No. 34).

Again, a drop of Gold H Bromide in Concentrated HCl or of Gold H Chloride in Concentrated HCl (the latter, however, much less sensitive) may be added directly to a little dry physostigmine or its salt.

Method of Direct Application

With the use of a test drop of concentrated HCl, or other strong acid, it is possible (as in the morphine and physostigmine tests) to make crystal tests, in general, by adding the reagent directly to a little of the dry alkaloid or its salt. Direct addition may be used even

*A test in aqueous solution has been given, since this was written, by C. H. Wagenaar. *Pharm. Weekblad, 76,* 276 (1939), *C. A., 33,* 4375 (1939). The reagent: Lead iodide in concentrated Sodium Acetate solution.

with neutral or basic reagents for a few water-soluble bases and various alkaloidal salts (as in distinguishing cocaine and novocaine hydrochlorides by borax solution). With the precipitating agent dissolved in strong acid it is an entirely general method, for enough of the alkaloid or amine will then dissolve to provide for precipitation at varying concentrations throughout the test drop.

This new method and new series of reagents are so important that a more complete discussion, with formulas, must be deferred to a separate article. Their value may be illustrated by the identification of caffeine, theobromine, and theophylline with Gold H Chloride in concentrated HCl, probably the best microchemical test known for these alkaloids. Each gives different and characteristic crystals with this reagent. Gold H Bromide in concentrated HCl is possibly even more valuable for alkaloids and amines in general. The formula published for use on morphine may be used (4). For direct application the reagent need have only about one-third the concentration of the precipitating compound used in the reagent applicable to solutions.

The precipitating agents of most value in the strong acids are $HAuBr_4$, $HAuCl_4$, H_2PtBr_6, and KI_3.

Gold H Bromide ($HAuBr_4$) *in syrupy phosphoric acid, Iodine-KI in phosphoric acid, and a few other precipitating agents in a test drop of this same acid, precipitate all amines.* A discussion of this important subject, with particular reference to amine and amide compounds not precipitated by the usual "alkaloidal reagents" in aqueous solution, must also be deferred to a separate article.

In the rest of this article it will be assumed that the alkaloid or amine to be tested is in solution; and, normally, in simple aqueous solution of the amine-salt; although of course any reagent can be tried in conjunction with any solvent with which it is compatible.

Classification of the Reagents

The following arrangement differs only slightly from the one given in the preceding article (1).

1. Reagents which merely free the alkaloid from its combination with acid, precipitating the free base.

Group A.

I. Basic reagents.

2. Reagents which combine with the alkaloids—

Group B. Oxygen acids.

II. Simple Oxygen acids (and their salts).

III. Complex Oxygen acids.

Group C.

IV. Halogen Reagents.

Group D.

V. Simple alkali Halides and Pseudohalides.

Group E. Halide and pseudohalide salts and acids of "central" metals, commonly double or complex acids or salts.

VI. Chlorides.

VII. Bromides.

VIII. Iodides.

IX. Cyanides.

X. Thiocyanates.

XI. Nitrites.

XII. Double Halides (chloro-bromides, etc.)

Group F.

XIII. Organic reagents.

I. Basic Reagents

This group, with the addition of borax and tri-sodium phosphate, has now been pretty thoroughly explored.

Alkaline reagents, such as Nessler's, which have a precipitating action in excess of that due to the alkalinity, are not included in this this group, but are discussed later.

II. Simple Oxygen Acids

To this group has been added chloro-chromic acid, a connecting link between the oxygen acids and the complex chlorides, precipitating agent $HCrO_3Cl$.

The writer has been unable to try perrhenic acid, which has been given as an alkaloidal precipitating agent (10) (11). However, it is doubtless similar to permanganic acid.

III. Complex Oxygen Acids

The intricacies of this class of compounds (the most general of the precipitants for aqueous solutions) are not altogether unravelled. According to Mellor (12) molybdic and tungstic acids form phospho-, arseno-, arseni-, vanadi-, and silici-complex acids. Boro-tungstic and phospho-antimonic acids have also been recognized as alkaloidal precipitants (13), and phospho- and arseno-vanadates exist (14). Chromium is in the same series with molybdenum and tungsten and is said to form complex acids also (12), but the writer has not found any effective chromium compound of this class, and knows of none reported.

Very few of these possible compounds have been really studied. Phosphomolybdic acid (phosphori-molybdic would be a better name) is one of the best known, but only the yellow compound, approximately $P_2O_5.20MoO_3.51H_2O$, has been previously considered. With a large proportion of phosphoric acid the solution is colorless; and whether this is a different complex acid, or merely a solution of molybdic acid in phosphoric acid, its properties as an amine-precipitant should be studied. Neither of these phosphomolybdic acid reagents corresponds to yellow arseni-molybdic acid, but yellow phosphomolybdic acid with an excess of H_3PO_4 does. This last mentioned solution is unstable; a freshly prepared solution of phosphomolybdic acid is decolorized at once by adding H_3PO_4 in excess of about 0.7 cc. per gram, but an old solution—at least one made with some nitric acid—withstands a considerable addition, and remains yellow for at least several days. Adding 0.75 cc. syrupy H_3PO_4 to 5 cc. of a "stabilized" 10 per cent. phosphomolybdic acid solution produces a yellow reagent, giving crystals with narceine like those given by yellow arseni-molybdic acid (No. 13).

Adding phosphoric acid alone to sodium molybdate solution never produces a yellow color. If only a little phosphoric acid, corresponding even very roughly to the formula $P_2O_5.20MoO_3$, is added, and the solution acidified with HNO_3, HCl, or H_2SO_4, it becomes golden-yellow; but if much phosphoric acid has been used—about 0.7 cc. per gram sodium molybdate, or more—no yellow color can be developed.

Arsenic acid (As_2O_5) with sodium molybdate shows similar phenomena, though the molecular proportion of MoO_3 for the maximum yellow color is lower (about $As_2O_5.12MoO_3$).

Phosphotungstic acid is now a commercial article, assigned the approximate formula $P_2O_5.24WO_3.xH_2O$ (13). The formulas,

however, for making the reagent from sodium tungstate, utilize far more sodium phosphate or phosphoric acid than corresponds to this; Scheibler's formula, used by Stephenson (15) and others, is 6 to 8 grams sodium phosphate to 10 grams sodium molybdate, with 50 cc. water, acidified with HNO_3. Apparently this does not, after all, differ much in results from the theoretical acid, but it does tend to age to a reagent which will give crystals with narceine like the yellow phosphomolybdic acid with excess H_3PO_4 (No. 11) which has been mentioned.

Thus the equivalence of these oxygen acids is something like this:

a) Ordinary yellow phosphomolybdic acid ($P_2O_5.20MoO_3$—No. 14, 1st series) = Ordinary phosphotungstic acid ($P_2O_5.24WO_3$—No. 15, 1st series).

b) Yellow arseni-molybdic acid (No. 13) = Arseni-tungstic acid (No. 15) = Stabilized yellow phosphomolybdic acid with H_3PO_4 or H_2SO_4 (No. 11) = Phosphotungstic acid aged with excess H_3PO_4 (No. 16).

c) Colorless phosphomolybdic acid (No. 12) = Colorless arseni-molybdic acid (No. 14).

The acids under (a) are the most effective precipitants, those under (b) are slightly less effective, those under (c) very much less.

The writer has not been able to study all the complex oxygen acids. Borotungstic acid is somewhat similar to silicotungstic; but what are the properties, uses and value of such other reagents as vanadi-molybdic, arseni-vanadic and phospho-antimonic acids? We may hope that some investigator will give us, some day, a complete account of this whole class of reagents. The foregoing account of the phosphori- and arseni-molybdic and tungstic acids will, however, show the difficulties attending the subject.

Alkali salts of the complex oxygen acids have very little specific precipitating action. Stephenson used sodium phosphomolybdate, and obtained precipitates with 26 alkaloids out of 51 (15), but the solution is alkaline to litmus, and the same alkaloids, for the most part, are precipitated by simple basic reagents. Sufficient acidity in the alkaloidal solution changes the reaction in the test-drop to that of phospho-molybdic acid; it rarely happens, therefore, that any amine

is precipitated by sodium phosphomolybdate as such. It can be dropped from the list of reagents with no appreciable loss.

IV. Halogen Reagents

Wagner's Reagent

The solution of iodine in potassium iodide is known under the names of various investigators, as Bouchardat's reagent, Kippenberger's, Kuehne's, Wagner's, Wormley's (16) and even others. Their formulas do not differ greatly, the weight of KI ranging from 2 to 5 times the weight of the iodine. The name "Wagner's reagent" was the one used by Stephenson (15), and is probably the most familiar; at any rate the writer previously used it as a generic name for the I-KI reagents, but distinguished eight different reagents, each containing 1 gram iodine, with from 1 to 50 grams KI in 100 cc. water.(1) These have all abundantly proved their value. Anyone interested in microchemical identifications, and still doubting the value of iodine reagents highly concentrated in KI, should look at the crystals given by Wagner's No. 7 or No. 8 with homatropine, hyoscyamine, atropine, and scopolamine—to mention only a group of related alkaloids.

The present article includes formulas for "Wagner's" reagents with an even higher ratio of KI to I than No. 8; these are not, however, of equal value with the eight varieties previously given.

Formulas for iodine-KI in acetic, hydrochloric, sulfuric, and phosphoric acids are also necessary, especially as reagents for direct application to the solid alkaloids. However, these will not be given here as the formulas need further working out and are somewhat outside the scope of this article, and the reagents will not keep very long. Formulas for six such reagents, specially devised for the identification of traces of morphine, but useful for other alkaloids as well, have been published recently by the writer (6). Also, the aqueous iodine-KI reagents can be applied to solutions of the alkaloids in the various acids, in the manner previously described.

Other Iodine Reagents

Iodine alone (without iodide) is much more soluble in acetic, hydrochloric, and hydrobromic acids than in water.

Iodine in hydrobromic acid seems to offer possibilities as a reasonably permanent acid iodine reagent, with its own particular crystal

forms and other characteristics. However, it cannot possibly supplant strongly acid forms of the I-KI reagents in all cases. Two formulas for Iodine in HBr are given, differing primarily in the strength of the acid, not in the ratio of iodine to HBr.

Iodine in concentrated HCl is not sufficiently general or sensitive to be of any value with the ordinary alkaloids. Iodine in acetic acid is not very general or sensitive either, but it will have a limited use, and accordingly a formula for the reagent is included.

V. Simple Alkali Halides and Pseudohalides

Previously 5 per cent. KI and 5 per cent. NH_4SCN were included with the complex metallic iodides and thiocyanates respectively; it now seems better to have them in a separate group. Metallic double salts are sometimes compounded with high concentrations of KI, NaSCN, or $NaNO_2$; hence these salts are not only alkaloidal precipitants in their own right, but are also needed for comparison and check on some of the results obtained with double salts.

Group E

DOUBLE OR COMPLEX SALTS AND ACIDS OF CENTRAL METALS

It would be interesting if someone with access to compounds of most of the elements would determine the exact limits of this group.

The metals concerned are those central to the "long periods" of the periodic table. With these periods written linearly, and the metals underlined which are known to be unmistakably effective in compounds of this kind in precipitating alkaloids, the boundaries of the class are, possibly, shown by the dividing lines:

A K Ca Sc Ti V	Cr Mn Fe Co Ni Cu Zn Ga Ge As Se Br
Kr Rb Sr Y Zr Cb	Mo Ma Ru Rh Pd Ag Cd In Sn Sb Te I
X Cs Ba $\left(\frac{\text{La}}{\text{Lu}}\right)$ Hf Ta	W Re Os Ir Pt Au Hg Tl Pb Bi Po 85
Rn 87 Ra Ac Ac Pa	U

As for the anion components, reagents in use are chlorides, bromides, iodides, cyanides, thiocyanates, and nitrites. Selenocyanates could undoubtedly be used, probably tellurocyanates, and possibly

fluorides. Cyanates, decomposed by acid, perhaps could be used in certain cases in precipitating the free alkaloids.

Birkenbach and Huttner give the following radicals as having a halogen character (17):

CN, OCN, SCN, SeCN, TeCN, $N(CN)_2$, $C(CN)_3$, CNO, N_3 and $C(NO_2)_3$.

There are also double halides or complexes such as chlori-bromides, chlori-nitrites, cyani-iodides and so on. Two such reagents were included in the preceding article, $Na_2HgCl_2Br_2$ and $Na_2HgCl_2(NO_2)_2$ but were classified with the bromides and nitrites respectively. For the present article such compounds are put together in a separate group, XII.

VI. Chlorides

The series of gold chloride reagents, made with different acids, is given, although for most of the precipitating compounds such reagents are omitted, pending further study.

VII. Bromides

Additional experience has shown that bromide reagents are indispensable. While similar to chlorides, they have numerous points of superiority, both as to sensitivity and crystals. They reach their greatest usefulness, it is true, in concentrated-acid test-drops; but even for aqueous test-drops a bromide reagent corresponding to nearly every chloride is abundantly justified. Among Stephenson's 35 reagents (15) there were no bromides, and very few have been used in the past by other investigators; five formulas for bromide reagents (not counting Mercuric Na Chloro-Bromide) were given in the writer's previous article; now 14 more are added. Series of gold bromide and of platinum bromide reagents, made with different acids, are given.

VIII. Iodides

Mayer's and Valser's Reagents

The Mercuric potassium iodide reagent seems to be usually called "Mayer's reagent," Mayer having done most to introduce and popu-

larize it. It has been pointed out (18) that Valser advocated the most sensitive form of the reagent, while Mayer used a formula, $HgCl_2$ plus 6 KI, containing excess KI, and therefore noticeably less sensitive. Neither Mayer nor Valser was the first ever to use such a reagent.

The reagent advocated by Valser is the same as the one previously termed "Concentrated Mayer's" by the writer, so that it might more appropriately be named "Valser's Reagent." "Mayer's" however, as the best known name, might well be retained for the standard reagent (less concentrated than Valser's), and for the convenient designation of some varieties, as "Acid Mayer's" and "Mayer's & KI." Stephenson called his mercuric potassium iodide reagent "Mayer's" (15), and made it with $HgCl_2$ and KI, but had it saturated with HgI_2. This is necessary for sensitivity; the standard form may be made with either $HgCl_2$ or HgI_2 without much practical distinction, but must be saturated with HgI_2.

In Mayer's reagent the mercury is present as K_2HgI_4 or $HgI_2.2KI$. In highly concentrated KI solutions saturated with HgI_2 the proportion is $2HgI_2.3KI$. This throws out HgI_2 on dilution. Valser, doubtless by intention, used as concentrated a solution as is practical. It will throw out just a little HgI_2 when diluted. However, by adding just enough "excess" KI to prevent any decided precipitation of HgI_2 in the usual test drop, it is possible to have a reagent several times more concentrated than Valser's. Such is the "Concentrated Valser's reagent" introduced here. It has enough KI to be just about midway between $2HgI_2.3KI$ and $HgI_2.2KI$.

It should not be surprising that Mayer's, Valser's and the Concentrated Valser's reagents will give different results in certain cases, for they differ not only in concentration, but in the mercuric compounds present.

Nessler's, and Alkaline Reagents

Nessler's reagent has not (within the writer's knowledge) been previously recommended as a general alkaloidal precipitating agent; but it is one, markedly more sensitive towards insoluble alkaloids than alkali alone, and with soluble-free amines in some cases even more sensitive than Mayer's reagent. The last is true, for example,

with pyrrolidine; but in most cases Nessler's reagent is less sensitive than Mayer's.

Nessler's reagent is generally described as alkaline mercuric potassium iodide, made by adding alkali to a solution of K_2HgI_4. However, the A. O. A. C. makes it by dissolving HgI_2 in NaOH solution (8b). It may also be made by dissolving HgO in KI. These methods all seem to result in much the same reagent. The one last mentioned reveals the compound in solution as $HgO.4KI$—or, since the solution is strongly alkaline, presumably $K_4HgI_4(OH)_2$. This method gives the best reagent for crystals, although mercuric potassium iodide solution plus alkali gives good results, the A. O. A. C. reagent being the poorest.

The effect of Nessler's reagent varies considerably with its concentration, and four different varieties have been distinguished, the classification being based on the crystals with atropine and hyoscyamine. Two varieties of alkaline mercuric potassium iodide are also given. Atropine and hyoscyamine also yield quite different crystals by reaction of the free base with neutral Mayer's or Valser's reagent.

Mercuric sodium cyani-iodide is naturally alkaline; it cannot stand more than feeble acidification without decomposing, and if made neutral or faintly acid, returns to alkalinity on standing. However, since it can be made temporarily neutral or even feebly acidic, it is not always nor necessarily an alkaline reagent. It gives good crystals with morphine. Mayer's reagent itself, incidentally, shows some tendency to become slightly alkaline on long standing.

Possibly other alkaline reagents of value can be discovered, aside from basic compounds which merely precipitate the free alkaloids, but none are evident at present.

There is one traditional alkaline reagent, sodium tannate. Although commonly referred to as the "tannic acid" reagent, tannin is far more effective in neutral or slightly alkaline solution than in acid. Mulliken combined it with Na_2CO_3 in testing for basic dyes (19); in other cases, including the formula previously given by the writer, sodium acetate is added to produce neutrality. It can be used in strong alkali. However, tannin does not give crystals and therefore has small value in any form.

Mercuric bromides and chlorides are not compatible with strong alkali but could be used as follows:

$NaHgBr_3$ with 2 per cent. borax
$HgBr_2$ (5%) and NaBr (20%) with 1 per cent. NaOH
$NaHgCl_3$ with 5 per cent. Na_2HPO_4
$HgCl_2$ (5%) and NaCl (25%) with 1½ per cent. Na_2CO_3 or Na_3PO_4.

These are not given with the formulas in the following part, since no definite practical uses have been discovered for them and their value is problematical.

It is obvious that the compound combined with alkali must not only be compatible, but also more effective than alkali alone, if the combination is to have any value.

IX. Cyanides

The Ferrocyanide reagent was previously given as its potassium salt, although, as was mentioned, it is likely to act as a basic reagent. Indeed, the cinchonine crystals described by Stephenson as given by potassium ferrocyanide, and which he considered the second best test for cinchonine (15) apparently must have been the free base thrown out by an unusually alkaline reagent. The true ferrocyanide crystals with cinchonine (yellow plates) require a decidedly acid test-drop. An acidified solution of the potassium salt may be used, but not any acid in any proportion: acetic acid is ineffective; mineral acids in the proper proportion give good crystallization with cinchonine, but with cinchonidine phosphoric acid is incomparably better for crystals than sulfuric or hydrochloric.

The precipitates of the alkaloids with hydroferro- and hydroferricyanic acids were the subject of extended studies by Cuming and Brown (20).

The mercuric cyanide reagent seems to have the rather surprising formula $H_4Hg(CN)_6$, and is remarkably stable—at any rate the writer's solution has been kept nearly a year and is still effective, although it has turned brown. This reagent has to be acid to show its distinctive characteristics, otherwise the free alkaloid is precipitated instead of a complex cyanide. This interesting reagent is not sufficiently general or sensitive, and too dangerous to make and use, to have any great value.

No cyanide, in fact, is an especially good precipitant, but several are useful with alkaloids that are fairly easy to precipitate.

(To be Continued)

PUBLIC SPEAKING FOR PHARMACISTS

By Frank B. Kirby

THERE seems to be a growing desire and possibly a growing demand for public speaking. An increasing number of clubs, societies, groups and associations are apparently always "in the market" for speakers. The growing demand is both on the part of speakers looking for invitations and groups looking for speakers. Witness the many classes in public speaking in day schools, night schools, day colleges and night colleges. In fact right now there is at least one medical and one pharmaceutical journal each giving a series of papers of instruction in public speaking.

Whatever may be back of this interest, too few such students carry on to an effective finish. Here is one study that cannot be perfected by reading or in a correspondence course. It definitely requires practical work. You may get the principles as above but the practical test requires platform experience.

It would seem the need at this time is a matter of encouragement for both you who have studied public speaking and never used the knowledge and you who hope to study it some day.

Following the Benjamin Franklin plan we must first study the cost and its possible value. If the cost is too high or you are not willing to sacrifice for what you get and (or) if the returns are not what they look like on the surface, then we know what to do.

First what are the costs? Seldom is a text book necessary or even desirable. Books have their value but an experienced teacher is your first consideration after having decided in favor of the study. Some might start the opposite way and list the advantages first. Mostly, however, decisions are made on the cost basis. There will be a fee for the teacher unless you may join a night high school or an adult education class paid for under the Deen Act or other government set-up. A one man class may look like the equivalent of tutoring instruction but really what you definitely need is a class by which you get the advantages of a critical, yet sympathetic, audience for your practice work.

The largest cost element is your time, not much but enough. These three possible charges, therefore, must be considered—first a text book, second the tuition or teacher fee and third the time

*Director of Education Abbott Laboratories, Chicago, Ill.

element for class work and practice. After having decided on and secured the former it is very necessary to find your audiences.

I have known people to take class after class hoping some day to find some audiences. The urge or desire continues and remaining unsatisfied they think another class of instruction will fill their requirements. The fact is one must be exposed or rather expose one's self else how does an audience or group know you can speak?

Suppose we first plan the talk and then plan the approach. One of the splendid slogans of the late Doctor Sheldon of the Sheldon School of Business is "know yourself, know your goods, know your customer." You must know your capacity and your limitations. Writing from an experience of years before a thousand audiences, I know that capacity and limitations are flexible. You may enlarge the one and reduce the other. As you increase your capacity by study and experience you reduce your limitations and change the character of both your presentation and your audiences.

It is my pleasure to emphasize to many a high school group the importance of their high school studies as foundation work very necessary to a better understanding of subsequent college work. Too many college students, men and women, in medicine, pharmacy, the arts and other subjects, look to their work as having one objective, namely, an end in itself or final in a State Board or other official examination. Actually such studies form the background of your evaluation by a most critical audience, your prospects, who may become clients, customers or patients.

Your four-year pharmacy course with, at times, post graduate work, gives you something basic to your future success not alone by way of cultural advantages. It would appear without fear of contradiction that the curriculum of a course in pharmacy gives you a wealth of subjects in which the public is interested. Before finding the public we might better prepare the talk.

Suppose you want to talk on "our imported materia medica" or "Round the World Contributions to our Health" or "The Pharmacist Imports Botanical (or Metallic) Medicinals" or "Foreign Medicinals for Domestic Consumption." You plan to use some facts you learned at college and as a memory refresher you look up some of your books. Read them several times marking what you want in your talk. Then write out your subject. To get the length of your paper have someone time your delivery speed, while you read anything, the daily paper or a drug journal. So many words per minute

and say you have a thirty-minute speech to assemble and in this way you know how many words you will need.

Now you have the complete paper. Maybe you write it several times. You certainly read it several times and then mark the salient points, the natural divisions of your subject. Write them down as the skeleton of your speech. Then see what you can do in reciting your speech from the skeleton outline. Practice and practice until you can reduce even the outline and then you are prepared for your audience. Do this for two or three speeches as you may have a return engagement. Who can tell?

The Franklin method counts not only the cost but the possible returns. So we make a survey for audiences. What kind of groups might be interested in your subject. You might analyze your prospective groups first and then build your talk. In this way you will find churches, schools and clubs of various kinds. You will locate a dozen or so varieties of luncheon service clubs, boy scouts, girl scouts, hospital training schools, P. T. A. groups and so forth. Contact your Chamber of Commerce for a list of clubs with days, hours and places of meeting. A letter or a personal call is probably all you need to secure an invitation. Rarely is a fee offered for this type of service. Seldom even do they expect to pay your car fare. Therefore your returns other than personal satisfaction in a good job well done will be confined to such promotional values as you can develop.

Compare these returns with the problematic dividends from your best window display and you will find it pays. On a basis of painless advertising this type of high grade promotion has tangible values. For instance on a basis of pure service to service clubs I have traced definite cash register results within ten minutes of a luncheon talk. This was accomplished while holding their good will as a repeat invitation will testify.

The results are there so do not add to your costs by instituting any survey to prove profitable returns.

Four years in a Pharmacy College plus experience give you a lot of information on prescription writing. How many of your dentists write prescriptions? Why do not the others? Here is your big chance to develop a lecture course of a few platform contacts by which in a practical way you show them the logic and technic of prescription writing to your and their advantage.

It would be interesting to know how many pharmacists are giving a course of lectures on pharmacology and materia medica to a nearby nurses' training school. It would be more interesting to be the happy promoter in starting many another pharmacist in this attractive profit builder as they take on this type of work to their personal advantage. Remember the Sheldon slogan—"He profits most who serves best." Rarely will such a position pay a fee but there are hidden values which mean pay dirt from the start.

A director of a nurses' training school told me she was teaching anatomy, physiology, pharmacology and materia medica. I questioned how she could cover so much and suggested she should have a larger faculty. Her answer was to the effect that teachers were difficult to find. If she brought in a physician to lecture on pharmacology he would emphasize just those drugs which he mostly prescribed, thereby reducing the scope and value of that particular subject.

What is the situation in your hospitals? Here may be opportunity knocking at your door. Picture the asset to you in such a connection sure to be known to many a physician, dentist and nurse, possibly all in your operative area which is thereby enlarged by just so many more personal contacts. Public speaking for pharmacists can be made to pay.

Is there anything in your store that has a story which might interest your high school seniors like iodine, sulphur, sodium chloride, iron, arsenic, and other chemicals common to you but having real romance if you develop the story?

What about the possibilities in a lecture on animal drugs or gases used in surgery like ether, ethylene, nitrous oxide and others?

We have the subjects of interest to an inquiring public; we have the man power as shown by our many graduates from a four-year pharmacy course. It remains to capture the waiting public in this splendid way on the lecture platform to emphasize pharmacy and its attainments and possibilities.

THE COMMON COLD AND THE PHARMACIST

By J. Leon Lascoff

IT has been estimated by competent authorities that upon the day that a man is handed his medical diploma, there has been expended on his support and education $30,000. Some of it has been paid by his relatives or friends, or possibly by himself. The rest has been paid by the community in one form or another.

The community has been just as active in encouraging pharmacists to be as capable as they can. Today, in order to become a pharmacist, nine years of advanced education is required. Namely, four years of high school, four years of college, and one year internship in a pharmacy. Thus, in the case of both the physician and the pharmacist, when a state hands out a license or qualifying certificate, it says in effect, "We are giving you this license in your chosen profession after having done everything humanly possible to make you competent—and this certificate represents to the people of your community that you are qualified to pursue your chosen field."

When a patient's life is in the balance, correct medication, properly compounded, may save that life and prolong its usefulness for a multitude of years. When a physician writes a prescription, it is the pharmacist, not the physician, who bears the final responsibility under law for its proper dispensing.

Diagnosis of the nature of a patient's illness is the function of the physician. Responsibility for the correct compounding of a prescription rests with the pharmacist.

Close to 200 million prescriptions are compounded annually by the pharmacists of the United States. Through the skill of the pharmacist in preparing these prescriptions, the lives of many millions of Americans are saved every year, and happiness is restored to millions of American homes.

True, an important part of our field consists in mutual consultation with the physician on matters pertaining to drugs and drug therapy. Nevertheless in the interest of public health, we must emphasize the fact that it is the physician's function to diagnose and treat the ailment—not the pharmacist's.

Many people who do not, for the moment think of the safeguards that our states have set up to protect those who live in them—

jump to conclusions about pharmacies. If you buy a bread at the bakery, you don't expect the baker to know whether you are permitted by your doctor to eat it; if you buy a bar of candy you do not expect the salesman to know whether your family physician has forbidden you to touch sweets by reason of some illness you may have had. Yet, when a man or woman walks into a pharmacy, he or she seems to feel that because the apothecary is surrounded by medicines, drugs and herbs at all times, he should know when they are to be applied in the cases of individuals.

In fact, some unreasonable people actually become angry when we explain courteously that our training has not qualified us to prescribe—that the State of New York has only licensed us to do the very important job of making up the prescription exactly as the physician ordered it, so that the individual for whom it is required will get the most good out of it.

It is not that we are in possession of medical secrets that we refuse to share with our customers. It is merely that we have been trained to make up medicines—*not* TO PRESCRIBE THEM. And for this same reason, the physician is qualified to prescribe—not TO DISPENSE MEDICINES.

At this time of the year, many people suffer from coughs and colds. In spite of all the efforts made by public health agencies to educate the public, many still insist upon ignoring the physician in this matter, and too often go to the pharmacy and purchase some preparation which they have heard advertised on the radio, or which they have read about in the newspaper or subway advertisements.

I believe that most pharmacists advise the people who call on them for medical advice, that in the long run it is better to consult a physician and receive competent treatment, than attempt to serve as their own physician. Someone has said that the person who serves as his own lawyer has a fool for a client, and I believe that it might also be said that the person who serves as his own physician has a fool for a patient.

There are many reasons why the pharmacist should advise that a physician be consulted whenever medical advice is requested. As a rule, pharmacists are honest and conscientious in their dealings; they realize that a sufferer's best interests can be served by a physician, and by no one else.

I believe that most pharmacists are instrumental in having people visit their physicians for medical treatment. In my experience,

I have seen persons suffering from colds, and other ailments, too, who stubbornly insisted that they did not wish to see a doctor. One young woman came to me and asked for something for a cough. I asked her how long she had been troubled by the cough. She told me that it had persisted for about five weeks, and I persuaded her to see a physician. Later, she came to thank me because the physician had found on examining her, that she had an early case of tuberculosis. She was treated and is now pronounced cured.

My suggestion to the layman is: Consult your physician. When he prescribes for you, go to your pharmacist who will compound the prescriptoin exactly as the physician ordered. Remember, that a prescription is a medicine designed especially for you—and for you only.

Dr. Fishbein Lists the Ten Big Medical Advances of 1939 as Follows:

1. "That sulfanilamide can halt or minimize numerous diseases.

2. That vitamin B_1 deficiency is widespread, and that the synthetic vitamin relieves nerve disorders caused by this deficiency.

3. That sex hormones alleviate some nervous conditions in both men and women passing through the climacteric.

4. That a new drug, Sobisminol mass, is a patent medicine that can be taken by mouth to help treat syphilis.

5. That vitamin K stops certain forms of hemorrhages.

6. That human beings can be refrigerated to a state of 'frozen sleep' which arrests cancer growth temporarily.

7. That repeated blood transfusions are an essential for treating severe burns successfully.

8. That swine may be the source of influenza epidemics by harboring the germs in latent form between epidemics.

9. That a difficult nerve-cutting operation on the spinal column can relieve severe cases of the heart disease, angina pectoris.

10. That surgeons can close an opening which prevents the start of blood flowing through the heart of some new-born babies."

—*The McNeilogram.*

ABSTRACTS FROM AND REVIEWS OF THE LITERATURE OF THE SCIENCES SUPPORTING PUBLIC HEALTH

Estimation of Traces of Lead and Thallium in Pharmaceutical Chemicals—A Simple Dithizone Limit Test. K. Bambach, *J. Ind. & Eng. Chem. Anal. Ed. 12*, 63 (1940). The dithizone limit test presents certain advantages over the heavy metal test of the United States Pharmacopœia XI and the lead test in the British Pharmacopœia of 1932. Although the test is not useful for extremely accurate analysis, it is applicable in routine analysis to insure that pharmaceutical chemicals and preparations do not exceed governmental specifications for lead. The test, based on acceptable photometric methods, is quite simple, rapid, sensitive, and specific for lead and thallium. The use of special equipment is not at all necessary. It is possible with this method to detect one part of lead and thallium in one million parts of any official chemical. It is believed that the dithizone method could supplant the present official procedure for detection of heavy metals, however, continuing the present official method for the less toxic metals.

METHOD.

Reagents—Although the presence of lead in the reagents is corrected for in the procedure, it is desirable to use deleaded reagents. The dithizone solution (12 mg. diphenylthiocarbazone per liter of chloroform) should be shaken with approximately one-half its volume of 1 per cent. nitric acid, the separatory funnel used for shaking then being used throughout the test. When storing, the reagent should be placed in a wrapped pyrex bottle and kept in a refrigerator.

All other reagents should be suitably purified and all glassware (pyrex) should be cleaned with dilute nitric acid (1 + 1). All filter papers should be of quantitative grade and acid-washed.

Preparation of the Sample—In general, the sample is dissolved in a few milliliters of dilute nitric acid (1 + 1), boiled and cooled. There are a few exceptions or special procedures required. Of the ten special procedures reported, only two of these are given herein.

Bismuth Subcarbonate—Sample is dissolved, with the aid of heat, in a minimum amount of concentrated nitric acid. After adjustment of the pH, sample is heated on a water-bath, after which ammonium citrate, potassium cyanide, and hydroxylamine hydrochloride are added and the pH again adjusted. Lead and most of the remaining bismuth is extracted with a special dithizone solution (30 mg. of dithizone per liter of chloroform). This extract is then extracted with dilute nitric acid and sufficient ammonium hydroxide added to give pH 2. The bismuth is then extracted with dithizone solution and the aqeous layer treated as under "Estimation of Lead" except that only 3 ml. of ammonia-cyanide mixture is added.

Cod Liver Oil—Sample heated cautiously with 5 ml. of concentrated nitric acid and 10ml. of water; aqueous portion evaporated and the residue heated to 500 degrees C. The ash is moistened with nitric acid and ignited as before. This process is continued until the ash is almost white. The ash is then dissolved in 3 ml. of nitric acid and the lead determined.

Extraction of Lead—The prepared sample is placed in a graduated Squibb separator and ammonium citrate, potassium cyanide, hydroxylamine hydrochloride added. After making solution alkaline with distilled ammonium hydroxide, the solution is shaken with dithizone solution, the dithizone extracts then extracted with nitric acid and the chloroform layer discarded.

Estimation of Lead—To the above prepared sample, 5 ml. of dithizone solution and 4 ml. of ammonia-cyanide solution are added. The whole is shaken for 30 seconds and the color of the dithizone extract compared with standards.

Throughout the procedure thallium, if present, will follow lead but is not objectionable since it is as dangerous in pharmaceutical compounds as lead and its detection is equally important.

Tables are given comparing results obtained by these methods as well as numerous references. H. G. D.

The Effects of Intravenous Injections of Magnesium on the Human Heart. M. Bernstein and S. Simkins. *J. Lab. and Clin. Med. 25,* 131-141 (1939). Inasmuch as very little work is available concerning the parenteral effects of magnesium on the heart, and even more so in view of the increasing importance of magnesium as the agent of the circulation time test recently perfected by Bern-

stein and Simkins, the same authors have investigated the intravenous effects of *therapeutic* doses of magnesium on the human heart.

The effects of the rapid intravenous injections of 10 cc. and 20 cc. of 10 per cent. magnesium sulfate were recorded electrocardiographically in 100 patients. The three standard leads of the electrocardiogram were recorded prior to injections, simultaneously with the injection and one hour later. Thirty-five sets of tracings were taken in 34 noncardiac patients and 69 sets in 66 cardiac patients. The cardiac group included 28 persons with arteriosclerotic heart disease, 25 with hypertensive heart disease, 5 with only electrocardiographic evidence of cardiac disease, and a miscellaneous group of 8 cases comprising 2 persons with chronic rheumatic heart disease, 1 with postscarlatinal complete heart block, one with syphilitic dissecting aneurysm of the aortic arch, 2 with congenital heart disease, 1 with subacute bacterial endocarditis, and 1 with hyperthyroidism.

In the noncardiac group, 6 patients presented minor T and QRS changes (usually in one lead) both during the injection period and subsequently; 4 showed similar changes one hour after injection. In the cardiac group similar changes were exhibited by 6 persons during the injection period, by 15 persons one hour after injection, and by 5 persons both during the injection period and one hour later. The striking feature is the complete lack of uniformity of changes wrought upon the heart by magnesium. Careful study of the findings indicates that these changes are negligible and that the rapid intravenous injection of 10 cc. to 20 cc. of 10 per cent. magnesium sulfate exerts no deleterious effect on the human heart. The coincidental administration of digitalis yields no untoward effects. M. B.

Notes on the Stability of Acetylsalicylic Acid. H. W. Tomski and L. J. Waller. *Pharm. J. 90,* 53 (1940). The subject of the stability of solutions of acetylsalicylic acid dissolved with the aid of ammonium acetate, potassium citrate and sodium citrate has been fully discussed in a paper by Morton (*Quart. J. Pharm. Pharmacol. 6,* 493 (1933). The following describes experiments on suspensions and alcoholic solutions of acetylsalicylic acid.

Suspensions of acetylsalicylic acid were prepared by adding 1.5 gm. to sufficient water to make 50 cc. A series of such suspensions was left undisturbed under ordinary laboratory conditions and the per cent. decomposition determined at various intervals. In a like manner the per cent. decomposition in a 3 per cent. alcoholic solution

after various intervals of time and that in a 3 per cent. solution of acetylsalicylic acid in solution of ammonium acetate were determined.

The per cent. decomposition at any time t was calculated from the formula % decomposition $= (\frac{y-x}{x})$ 100 where x = cc. standard alkali required to neutralize acetylsalicylic acid at zero time and y = titre at time t.

The results indicated that in 50 per cent. alcohol the loss of acetylsalicylic acid was about 1.5 per cent. per day, 6.0-6.5 per cent. per week and about 13.5-14.5 per cent. per month. A suspension of the same strength lost 0.3 per cent. per day, 1.6-2.0 per cent. per week and 7.0-8.0 per cent. per month. In acid-alcohol solution and solution prepared with ammonium acetate the decomposition was much greater.

The authors conclude that suspensions should be prescribed and dispensed in preference to solutions regardless of the method of obtaining such solution. L. F. T.

The Detection and Estimation of Benzedrine. E. T. Illing. *The Analyst, 65,* 3, 1940, No. 766. Benzedrine (Amphetamine, N. N. R.) or β-aminopropylbenzene with the formula ($C_9H_{13}N$) is chemically allied to ephedrine and adrenaline. Its action is to diminish gastro-intestinal activity, raise blood pressure, interfere with sleep and in some instances cause pronounced psychological changes.

Contraction of the blood vessels and shrinkage of the membrane occurs when benzedrine is applied to mucous membranes. Benzedrine is employed in coryza as an inhalant to free congested nasal passages.

It has a tendency to abolish fatigue, particularly in depressed patients. A case of self-administration of 190 mg. of the drug over a period of 19 days produced an acute aplastic anaemia with severe cardiovascular collapse on the day following the last dose. Recovery was very slow.

The author presents results of a study made on the detection of the drug in viscera as a result of a case of sudden death due to hemorrhage in the cranium. Physical characteristics of benzedrine reveal a liquid completely volatile at 100 degrees C. and appreciably volatile at low temperatures such as 33 degrees-35 degrees C. The acetate also is volatile. It is slightly soluble in water, more soluble in alco-

hol, and readily soluble in acids, ether, amyl alcohol, ethyl acetate and chloroform. Its hydrochloride, sulphate and tartrate are crystalline in nature, non-volatile and do not decompose when heated at 100 degrees C. All are soluble in water and alcohol (especially 50%), the chloride and tartrate being more soluble than the sulphate.

The extraction of benzedrine from solution with chloroform must be done in the presence of alkali. Use of sodium bicarbonate requires a large number of single extractions. The method finally adopted is as follows: "The aqueous (generally acid) solution, containing in 50 to 100 ml. the benzedrine salt, is neutralized approximately with 10 per cent. sodium hydroxide solution, and 1 ml. is added in excess. The solution is extracted with successive quantities (25, 15, 10 and 10 ml) of chloroform. Each chloroform extract is washed with the same 5 to 10 ml. of water, this wash water is then shaken with a little chloroform, which is added to the combined extracts, and the whole is washed with 5 ml. of water. The benzedrine is then re-extracted from the chloroform by shaking with four successive portions of 10 ml. of $N/_2$ hydrochloric acid. These acid extracts are evaporated to dryness on the water-bath, and finally the residue is dissolved in absolute alcohol, filtered into a tared flask, evaporated to dryness, dried and weighed."

Benzedrine gives the general reactions for alkaloids, such as those of Mayer and Dragendorff. It does give a purple color in the modified Mohler's test the conditions and precautions being the same as those used in detecting benzoic acid. The test is sufficiently sensitive to detect 0.1 mgm. of benzedrine and the color given by 1.0 mgm. is a convenient one to match in a volume of 15 ml. The color is quite stable if the following solution is used as a diluent: "Twenty ml. of conc. sulphuric acid are added to 40 ml. of water containing 2 g. of potassium nitrate, and the liquid is cooled while 200 ml. of water containing 100 ml. of ammonia (sp. gr. 0.880) are added carefully. Finally, 40 ml. of water containing 0.8 gm. of hydroxylamine hydrochloride are added. This solution may be used for diluting the final 15 ml. of the test solution to 50 ml. or other convenient volume. From 2 to 3 mg. of benzedrine in a volume of 50 ml. give a color suitable for matching. Ephedrine and adrenaline under the same conditions give a deep yellow and a slight yellow color respectively."

To distill the benzedrine 25 g. of the salt, 50 ml. of water and a sufficient quantity of sodium hydroxide to render the solution

alkaline are placed in a 1-litre round-bottomed flask, fitted for steam-distillation, no condenser being necessary. The distillate, small in volume, is passed through 10 ml. of N hydrochloric acid in a conical flask (200 ml.), connected by means of a glass tube with outlet of the distillation flask by rubber tubing; the other end of the glass tube passes through a bung in the neck of the conical flask. The distillate then passes through 10 ml. more of N hydrochloric acid contained in a distillation flask (100 ml.) and the glass tube leading into this flask is drawn out so as to make a slightly smaller orifice. Add sufficient water to the acid in each flask to form a seal allowing the steam to escape through a side tube in the last flask. Heat the main flask so that a small amount of salt remains undissolved, continuing the distillation for 30 minutes at which time stop the steam and disconnect the tube; disconnect the outlet of the main from the conical flask and *then* remove the flame. Evaporate the combined distillates to about 50 ml. and extract as above.

To extract the benzedrine from the viscera, use the Stas-Otto process but use tartaric acid to acidify if necessary. Extract the benzedrine with chloroform. To prove the presence or absence of benzedrine, extract with hydrochloric acid. In an unknown specimen render the solution alkaline with sodium bicarbonate and extract with chloroform. It is practically impossible to distill benzedrine from viscera because of excessive frothing.

In extracting benzedrine from the urine use steam-distillation as described.

Benzedrine is present in tablets as the sulphate. For accurate results convert the sulphate into the hydrochloride by taking a sample of 0.892 g. of crushed tablets, a small amount of solid $BaCl_2$ and 1 ml. of *N* HCl in a 100 ml. conical flask. Add 25 ml. absolute alcohol and heat the mixture on a water-bath for a few minutes. Filter and wash the residue with absolute alcohol which is then evaporated but not to dryness. Filter the liquid into a separator, wash filter with acidified water, neutralize filtrate with 10 per cent NaOH solution and add 1 ml. in excess. Extract with chloroform as above.

To extract the sulphate directly use 50 per cent. alcohol and continue as above, omitting the $BaCl_2$ and HCl step. Acidify the alcoholic filtrate with 2-3 ml. N/10 HCl.

Distillation is used as above, prolonged for an hour and using 1.4162 g. of tablets. "When 20 mg. of benzedrine were distilled only 18.8 mg. were recovered and, if this is made the basis of a cor-

rection, the 4.55 mg. per tablet found are equivalent to 4.9 mg. of sulphate per tablet.

Heat one or two crushed tablets of the sulfate with 25 ml. of water and 5 ml. of conc. HCl on a water-bath for 1 hour. Filter, wash residue and estimate sulphate in filtrate. Since the $BaSO_4$ is precipitated slowly, allow to stand several hours, preferably overnight. To complete precipitation in 3 hours, dissolve the tablets in 25 ml. of water containing 2 ml. of 10 per cent NaOH, heat on a water-bath, add 5 ml. conc. HCl and proceed as above.

M. O. H.

The Effect of Orange Juice on Calcium Assimilation. C. S. Lanford. *J. Biol. Chem. 130,* 87 (1939). Earlier workers have suggested that orange juice favors the retention of calcium. To test this a group of young rats was given a small supplement (5 cc. daily) of orange juice in addition to a basal diet of wheat and milk. A control group was given the basal diet without the orange juice. At the end of the experimental period each group was killed and the calcium content of the carcases was determined. By subtracting from each value thus obtained the average calcium content of male or female rats of the same age as the animals at the beginning of the experiment, a figure was obtained for the amount of calcium retained by each individual during the experiment. At the same time by analysis of the food a figure was obtained for the calcium consumed by each individual. From these two figures the percentage retention of calcium by each animal was calculated. In the group receiving orange juice the amount of calcium stored in the body was 8 per cent. greater than in the control group and the total calcium was appreciably greater. The improved assimilation was noted in every case and it is believed to be statistically significant. It was also noticed that growth in the group receiving orange juice was about 10 per cent. greater.

L. F. T.

Chemotherapy in Pneumonia.* H. C. Hinshaw. *Proc. Staff Meetings Mayo Clinic 14,* 769 (1939).

During the past year, our management of pneumonias has undergone radical revision. Although none of the older procedures have been repealed, new and effective weapons have been added.

*This article is reprinted in full since it is considered by the editor to be one of the best brief summations of the use of sulfapyridine yet to appear.

When these new methods have been adopted by the medical profession we may anticipate at least a reduction of 50 per cent in mortality from pneumonia. Realization of this hope and prediction will constitute one of the greatest accomplishments of medical science in many decades.

I refer, of course, to chemotherapy for pneumonia. Most authorities agree that sulfapyridine is the one chemical to use in treatment for the pneumococcal pneumonias. This group includes the vast majority of primary pneumonias, both of lobar and of bronchogenic distribution. It also includes most of the secondary pneumonias, that is, those which follow operation, acute infectious disease, trauma and debility.

We first received sulfapyridine for trial nearly a year ago, when very little was known about its value or its hazards. In the meantime, our department has had extensive experience with its use. Most of this experience has been with postoperative pneumonia, but treatment for this type is not greatly different from that for primary pneumonia except that management of the former is more complicated than management of pneumonia that occurs among persons who have not undergone surgical procedures.

Within a few weeks after receiving sulfapyridine, we had worked out a set of rules to govern its use. These rules have remained without important alteration to this date. It is interesting that other medical centers, independently, have worked out essentially the same rules of procedure. Further experience may require revision.

The first rule is that, in cases of pneumonia, adequate dosage is essential to treatment with sulfapyridine. Smaller doses may be totally useless. There seems to be a threshold of efficacy. Half the full dose is not half so effective as the full dose and may be totally useless. This is not a therapeutic agent which may be tried cautiously or tentatively. It must be used boldly or not at all. Pneumonia is a true medical emergency that requires prompt, even drastic, treatment. Knowing the serious prognosis, we may even be willing to subject the patient to some hazard and to considerable discomfort for the sake of effecting recovery.

The minimal dose of sulfapyridine for adults who have pneumonia seems to be about 90 grains (6.0 gm.) a day. To elevate promptly to an effective level the concentration of sulfapyridine in the blood we usually double the first dose or both the first and second doses or even give four times the usual dose at the start. This

means that the patient will usually receive about 120 grains (8.0 gm.) during the first twenty-four hours.

The second rule is also important. Dosage must be well distributed throughout the day and night. Regardless of how greatly he needs sleep, or how peacefully he is resting, the patient should be awakened for administration of the drug during the night.

The third rule is hardest to follow. The occurrence of nausea, or even of vomiting, should not dissuade the physician from continuation of needed therapy. Some degree of gastric disturbance nearly always is produced. Troublesome vomiting is frequent, but it does not indicate serious reaction to the drug and must be overlooked if good results are to be expected. If a dose is vomited within an hour, it should be repeated.

In treating, with sulfapyridine, patients who have pneumonia, watch the chart, do not watch the patient! If the temperature has fallen, that patient is responding very well regardless of how wretched he may feel or appear to be. Indications for discontinuing the drug must come from the chart, not from the patient.

Opinions differ as to duration of therapy. A fair minimum would be to continue administration of the drug for forty-eight hours after the temperature is normal. This will mean three to five days of treatment. Some patients will suffer a relapse after this time and some authorities recommend continuance of medication in decreasing dosage for several days to prevent a relapse. The dangerous but rare leukopenias usually come from prolonged dosage and we have been reluctant to continue sulfapyridine therapy for more than four to six days. If relapse of pneumonia occurs, it again responds if treatment is promptly given.

The next important rule is based on the fact that results are prompt. When used in cases of pneumonia, the drug may be abandoned if real benefit cannot be demonstrated on the chart within forty-eight to seventy-two hours. If the dosage is adequate and if concentration of the drug in the blood is reasonably high, definite reduction of fever, if it is going to occur, should be demonstrable in less than forty-eight hours.

It seems that absorption, inactivation (acetylation) and excretion of sulfapyridine are much more erratic than absorption, inactivation and excretion of sulfanilamide and neoprontosil. For this reason, determinations of concentration of the drug in the blood are routinely performed. Lack of absorption accounts for some failures,

but not for all. We do not know why some strains of pneumococci appear to be resistant to sulfapyridine.

Another rule: For the most part, sulfapyridine should be used only for patients who are seriously ill. I doubt the advisability of using the drug for patients who have influenza, the common cold, sinusitis or tonsillitis. In such cases, this treatment may be worse than the disease, not only more uncomfortable, but more dangerous. For these reasons, I much prefer the less toxic and more dependable drugs such as neoprontosil or sulfanilamide for respiratory infections other than pneumonia, if any chemotherapy at all for such cases is justifiable.

The outstanding results of proper sulfapyridine therapy in cases of pneumonia is prompt arrest of the pneumococcal infection. This is manifested by a sharp drop in fever, often with dramatic suddenness. When the first dose of the drug is large, a drop in temperature may be noted in four to twelve hours. In more than half of the cases, the temperature will approach normal within twenty-four hours. The results are fully as striking as those of serum therapy and are definitely more dependable, especially in cases of postoperative pneumonia.

Because of the minor toxic effects already mentioned, the patient's sense of well-being may not follow closely the signs of improvement indicated on his chart. The pulse rate decreases somewhat gradually. The physical signs of resolution of consolidation appear slowly during the next few days. Only when administration of the drug is discontinued may we expect a return of the patient's appetite and contentment.

Cyanosis, usually mild, often occurs as a result of administration of sulfapyridine. We do not regard this as of any serious portent and usually, we overlook it. However, accompanying pneumonia, cyanosis is easily confused with the cyanosis of anoxemia, but inhalation of oxygen should relieve the cyanosis of anoxemia.

The unpleasant reaction of vomiting has already been mentioned. More than half of all patients will be uncomfortable, even miserable, from this cause. Rarely are we forced to discontinue really needed sulfapyridine because of vomiting. The drug is comparatively insoluble; hence, it is impossible to give adequate doses in solution. The soluble sodium salt of sulfapyridine is now undergoing clinical trial here and elsewhere, but it has not been released

for commercial distribution. Patients are nauseated regardless of whether the intravenous or the oral preparation is used.

Dangerous and fatal reactions to sulfapyridine are rare, but the danger is very real. If these reactions are recognized early and if proper treatment is instituted fatalities will occur rarely.

Sulfapyridine, like other members of the sulfanilamide family, affects the bone marrow. Sulfapyridine is probably the worst offender of the group. Several cases of fatal agranulocytosis have been reported. For this reason, daily estimations of the number of leukocytes per cubic millimeter should be made. If decrease in the number of leukocytes is rapid, the drug is best discontinued. Agranulocytosis is usually related to prolonged dosage, although a definite element of individual idiosyncrasy is the real determining factor. If administration of the drug is stopped early enough, the leukocytes may increase steadily after a few days.

Hemolytic anemias have been reported in association with administration of sulfapyridine with rapid fall in hemoglobin. If, on recognition of the hemolytic anemia, a blood transfusion is given, recovery is the rule. Fever and rashes, toxic delirium and other temporary mental changes due to the drug, have been reported. It seems probable that any patient who has experienced any serious reaction from sulfanilamide should not receive sulfapyridine.

One reaction is peculiar to sulfapyridine. It is based on the insolubility of the drug. The inactivated acetyl sulfapyridine may crystallize out of solution in the renal tubules and form concretions which may seriously hamper renal function. This is first manifested by hematuria; hence, frequent urinalysis is advised. These deposits should dissolve gradually and not leave permanent effects if promptly recognized and if forcing of fluids and alkalis is instituted.

The indications for sulfapyridine therapy in cases of pneumonia appear simple. We would recommend its use in all cases of pneumonia, regardless of whether pneumococci are found in the sputum or not, and regardless of whether lobar pneumonia, bronchopneumonia, or secondary pneumonia such as may follow surgical procedures is present. Further experience may serve to qualify this broad statement.

Contraindications are vague and are based on suspicion and hearsay. We avoid the use of sulfapyridine when patients relate any experience that is suggestive of a definite idiosyncrasy to sulf-

anilamide. We have avoided the drug or have used it cautionsly for patients who have hepatic damage. We prefer to withhold sulfapyridine from seriously anemic patients until a blood transfusion has been given. We do not deny it to those patients who are seriously ill with pneumonia who initially are found to have a comparatively small number of leukocytes per cubic millimeter of blood.

Do not be misled into the belief that sulfapyridine is the one and only therapeutic agent for pneumonia. Oxygen therapy is still required in most cases of serious pneumonia and the most meticulous nursing care is indispensable. In cases of postoperative pneumonia, efforts must be undertaken to overcome the mechanical factors which have caused the pneumonia. The day of serum therapy is not done with, but the circumstances that demand its use have not been well defined. Sulfapyridine therapy and serum therapy should act synergetically.

Sulfapyridine is not an ideal chemotherapeutic agent, but it is the best available therapeutic agent for pneumonia. However, we hope for and anticipate the time when it will be superseded by a more satisfactory agent.

Manganese in the Treatment of Dermatologic Disorders. From Report of Council on Pharmacy and Chemistry. *J. A. M. A. 114,* 246 (1940). Manganese preparations for parenteral use have been marketed for over fifteen years for the treatment of various cutaneous disorders including pustular acne, acne vulgaris, furunculosis, etc. A report is given by Dr. Maurice Sullivan on the clinical use of a colloidal manganese hydroxide in forty-three cases of acne vulgaris, folliculitis, sycosis vulgaris and rosacea. The conclusion reached was that colloidal manganese hydroxide was of no value in the treatment of the diseases mentioned above, that no "tonic" effect was observed, and that no appreciable effect was produced on the amount of hemoglobin in the blood. L. F. T.

SOLID EXTRACTS

By Ivor Griffith, Ph. M., Sc. D., F. R. S. A.

Despite the form in which this information is presented it may be accepted as trustworthy and up-to-date. Original sources are not listed but they may be obtained upon request.

Someone recently asked me how our grandmothers came to know so much about the medicinal virtues of herbs and simples. The answer of course was that they were the findings of experience, or in today's language, and practice, of experiment. What might be of more interest is to conjecture as to how we have come to *forget* so much of the art and knowledge of the ancients in these and in other matters.

Indeed, despite our so-called regimented research, we still discover much by the simple process of observation. For instance, in an inquiry to find why beer-drinking steel workers were more resistant to heat stroke than their teetotaler colleagues, it was found that the salt which the former put into their beer and consumed with their pretzels helped in maintaining a proper sodium chloride level in their blood in spite of large losses through prespiration. Even less obvious is the connection between vitamin A and accidents at night. This vitamin is necessary to the formation of "visual purple" in the eye, and therefore becomes an industrial aid by cutting down accidents caused by poor vision in dim light.

The studies of industrial fatigue that started with the intricate enough questions of physiology are now also dealing with sociology and psychology—even Freudian concepts. For instance, long-time studies of male workers indicate a certain cycle of work decline following the lunar cycle. Then, too, the labors of men between fifty and sixty were influenced by a definite menopause-like factor that indicate physiologic changes, much less acute, but just as certain in the male as in the female. Investigators show that men are not mechanisms in the engineering sense, and that the forces that restrict their enormous potential capacity for contentment and accomplishment cannot be overcome solely by measurable processes. Mother-in-law trouble mustn't nullify our new air-conditioning system.

Are you *pyknic* or *asthenic*. Listen, your shape shapes your future too, and whether you live long or short, depends not so much

on whether you are long or short, but rather upon whether you are thick or thin.

Among the results of a study, conducted by Dr. Raymond Pearl, the eminent Johns Hopkins investigator, the following points were emphasized:

Short-lived men who died of heart and kidney ailments were bigger around the body, in both chest and abdominal girth, than long-lived men who died of the same groups of diseases.

This condition was reversed in the case of men who later died of cancer and pneumonia: the skinny (asthenic) men were shorter-lived than the stouter (pyknic) type.

In those eventually dying from cancer and from diabetes the average body weight was also greater in the short-lived than in the long-lived group. The difference here, however, was too small to justify any very definite conclusions.

Height apparently had nothing to do with length of life. Talls and shorts were scattered at random through all the disease groups, among both long-lived and short-lived.

Colchicine, long known to pharmacists as the active principle in the wine of colchicum seed or corn, a preparation of ancient usage, is in the limelight. It is science's newest elixir to make plants produce giant offspring and go through other sudden and startling evolutionary changes, and also the finger of death to the abnormal tissue growths known as plant tumors.

At the great U. S. Department of Agriculture laboratories near Beltsville, Md., Dr. Nellie A. Brown has been experimenting with colchicine solutions as a means for getting rid of plant tumors without killing the plants. Using a wide range of experimental material, including tomato, bean, wild tobacco, four-o'clock, Paris daisy and French marigold, she has demonstrated that simply brushing on a solution of the drug (usually of 2% strength) will kill nine-tenths or more of all tumors treated. Injecting an even weaker solution into the tumor tissue with a hypodermic needle produces similar results.

Plant tumors, or plant cancers, as Erwin Smith called them, unlike the animal growths which they resemble, are caused by a microscopically visible germ, known as Bacterium tumefaciens. Colchicine does not kill this germ. The effect of the drug seems to be directly on the tissues themselves. Colchicine appears to be deadly to the plant

tumor cells, but not to healthy cells in the plant's normal tissues. Which challenges us to greater clinical trial on man.

Zephiran is, in chemical terms, alkyl dimethyl benzyl ammonium chloride. It is a powerful germ-killer suggested recently in the prevention and cure of that widespread disease dental caries. In addition, it acts as a cleansing agent, is relatively harmless to mucous membranes such as line the inside of the mouth, and it lowers the surface tension of water. This last property is important because it means the chemical is a good wetting and penetrating agent and can get into effective contact with the dense mass of germs in the dental plaque. Dental plaques are deposits on the teeth of material supposed to act as a medium for the lodgment of germs associated with the decay process. The product was developed, in an attempt to displace the mottling fluorides which had been found to be good enzymicides, but dangerous from other standpoints.

The so-called "pep pills" of benzedrine, resorted to, sometimes dangerously, by college students for wakefulness during cramming sessions, owe their sleepfighting effect to their influence on brain respiration, according to a recent article in Nature.

Benzedrine has "unquestioned value," the investigators point out, in the treatment of narcolepsy, that strange condition in which the patient is seized, often at inconvenient and even dangerous times, with the uncontrollable desire to sleep. The condition is also known as paroxysmal sleep or sleep epilepsy.

Many persons who have a tendency to sleep at the auto wheel carry the benzedrine inhaler to combat the dangerous drowsiness.

Synthetic glycerin, a product long sought in vain by chemical industry, is now available from petroleum.

Although glycerin is a simple organic compound, its molecular structure, with one atom of oxygen attached to each carbon atom, has baffled the synthetic manufacturer who must use processes of low cost. By allowing chlorine to react upon propylene, a gaseous component of cracked petroleum, California technologists have succeeded in producing at low cost the substance allyl chloride. From allyl chloride the compound trichloropropane is then readily prepared. The molecule of trichloropropane is similar in structural design to that of glycerol, and the product is readily convertible into glycerin with the aid of cheap alkali.

Cheap glycerin may make available new oils and greases, and it may not be long before we shall be producing a completely synthetic butter or other edible fat.

Areca nut and its alkaloid arecoline have long been used to vermipurge livestock. But now a chemical related to sulfanilamide, known as phenothiazine, has been found highly effective in the treatment of several species of parasitic worms in livestock by scientists of the U. S. Department of Agriculture. As soon as manufacturers make suitable application to the Secretary of Agriculture, it will be released as an accepted veterinary medicine.

In addition to its effectiveness against insects, worms and other cold-blooded forms of life, phenothiazine has been found to have marked fungicidal and bactericidal properties. In the latter field, it has been used as an internal antiseptic in human medicine, in the treatment of cystitis, pyelitis and allied diseases.

Three practical suggestions are these with acrostic technic, and perhaps a bit of impertinence, too:

WEED out the ambrosiacal ragweed. Destroy it in late July before it begins to infloresce, and save many a sneezetorn wretch from growling over the New Deal. The ragweed is 90 per cent. responsible for the hay fever in Eastern States.

POISON ivy, is another useless plant that might well be eradicated. Its annual crop of discomfort and agony is tremendously high. Human labor might be well dedicated to so worthy a proposition as this.

ARRANGE for a wider range of medicinal plants to be grown *here* instead of elsewhere. Whenever Europe leaves the hoe and hies to human slaughter many common drugs as belladonna, aconite, digitalis, etc., are at once upped in price and difficult to get. America can and should be self-sufficient in the necessities and dependent on no imports.

So might the W. P. A. do a great deal for the New Deal—and for U. S. generally.

No animal, except for the rat, is as omniverous as the human being. The stomach of man has been trained by a slow evolution to eat everything and because of this, man is to be found in all parts of the world. He can adjust himself to the foods of the cold Arctic regions as well as to those of the warm southern climates. In connection with this, it is interesting to note that the gorilla, a fairly close relation of the human, is limited to his little circle of territory because of the special diet which he requires.

The human animal has built up a highly complex mechanism as a result of nutritional requirements evolved a million years ago. Examples of special requirements of the human are noted in the vitamin field. The mineral requirements are complex, Iron and Copper being among the most important. The presence of copper in the human is probably a hangover from the time when man was a water animal and a basic copper salt was as necessary to its blood then as is the iron salt at the present time.

The demands of the body may be fulfilled through the use of vitamin preparations, extracts, etc., but the simplest and most effective way is to eat everything possible. But, unfortunately, the human has become finicky in food choice and as a result does not eat all foods to satisfy his specific needs. For example, animals and Eskimos eat liver, kidney, brain and entrails first. If they want more to eat they investigate the filet mignon. In case of the human, this process is reversed, if the pocketbook permits. As a result, the human does not get the necessary food factors, and the accessory eating of vitamins is accordingly quite rational and necessary.

Daffodils with blossoms as large as salad plates. Red tea roses with five-inch buds. Dahlias as large as umbrellas. Extremely dilute solutions of Vitamin B_1 (thiamin chloride) in water used on growing plants produced such effects in researches at the California Institute of Technology, and our flower shows a few years hence will more than likely.

In human beings this vitamin prevents and cures the serious nervous disorder known as beri-beri. In garden and field it is also useful. In addition to making plants grow vigorously and producing abnormally large flowers, this vitamin allows the transplanting of flowers and trees at any season. Concentrations as low as one part in 100,000,000 prevent "root shock" when flowers, shrubs and trees are transplanted.